REMARKS

Reconsideration of the Office Action mailed May 20, 2002, (hereinafter "instant Office Action"), entry of the foregoing amendments, withdrawal of the objection to claims 1 and 6, and withdrawal of the rejection of claims 1-8, 10, 11 and 46-51, are respectfully requested.

In the instant Office Action, claims 1-8, 10, 11 and 46-52 are listed as pending, claims 1-8, 10, 11 and 46-51 are listed as rejected and claim 52 is listed as allowed.

Attached hereto as Appendix A is a marked-up version of the changes made to the claims by the current amendments. Appendix A is captioned **"Version with markings to show changes made"**.

Applicants appreciatively note that the Examiner has withdrawn: the rejections under 35 U.S.C. §112, second paragraph; the rejection under 35 U.S.C. 102(e) over U.S. Patent No. 6,001,839; and the provisional obviousness-type double patenting rejection over Application No. 09/381,036, in view of the amendments filed on January 18, 2002.

Applicants also appreciate the allowance of claim 52.

The Examiner has rejected claims 1-8, 10, 11 and 48-51 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants have amended Claim 1 to remove the moieties "$-NHC(O)R_{130}-$" and "$-NHSO_2R_{130}-$" from the definition of variable "L". Amended claim 1 submitted herewith necessitates the amendment of claim 11 to remove "$-NHC(O)R_{130}-$" and "$-NHSO_2R_{130}-$" and to make it an independent claim. Applicants have also amended claim 11 to add back in the original moieties "$-NHSO_2R-$" and "$-NHC(O)R-$". Support for the newly amended independent claim 11 is provided by the fact that it was dependent upon claim 1 as originally filed and as such incorporates the limitations of claim 1 that are not specifically recited in claim 11.

Based upon the foregoing, the rejection of claims 1-8, 10, 11 and 48-51 under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Examiner has rejected claims 1-8, 10-11 and 46-47 under 35 U.S.C. 103(a) as allegedly being obvious over Calderwood et al. U.S. Patent No. 6,001,839 (hereinafter "the '839 patent"). Applicants respectfully traverse this rejection. The Examiner originally rejected

Applicants' claims over the '839 patent under 35 U.S.C. 102(e), which the Examiner has withdrawn. Applicants direct the Examiner's attention to 35 U.S.C. 103(c), which reads as follows:

> Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

The instant application was filed as a Continued Prosecution Application on February 13, 2001, and, thus, is an application covered by the provisions of 35 U.S.C. 103(c). The '839 patent is not prior art under 35 U.S.C. 102(a) or 102(b). The '839 patent was cited as prior art under 35 U.S.C. 102(e). As the Examiner points out at page 6 of the instant Office Action and pursuant to M.P.E.P. 706.01(l)(1) and 706.02(1)(2):

STATEMENT CONCERNING COMMON OWNERSHIP

U.S. Patent 6,001,839 and the claimed invention of the instant application were at the time the invention was made, subject to an obligation of assignment to the same person.

As further confirmation of the foregoing statement, Applicants have enclosed herewith the "Notice of Recordation of Assignment Document" for U.S. Patent 6,001,839, marked Exhibit A, (the Examiner will note that the assignment concerns U.S. Application No. 09/042,702, which is the application no. of the '839 patent) and for the instant application, marked Exhibit B. The Examiner will note that both the instant application and the '839 patent are assigned to BASF Aktiengesellschaft.

Accordingly, the rejection of claims 1-8, 10-11 and 46-47 under 35 U.S.C. 103(a) over the '839 patent is obviated and should be withdrawn.

The Examiner has maintained the rejection of claim 46 under 35 U.S.C. 103(a) over WO 98/41525. Applicants maintain the traversal of the rejection. Applicants refer the Examiner to the argument regarding this rejection which was filed in Applicants' Response mailed January 2, 2002. Applicants additionally point out the following.

The Examiner states at pages 6 and 7 of the instant Office Action that:

> ...the instant compounds have a fluoro substituent on the phenyl whereas the reference discloses species wherein the phenyl is substituted by methoxy or hydroxy. The reference, however, teaches the equivalence of methoxy, hydroxy, fluoro, etc. by disclosing them as alternatives on the phenyl ring. Further, the instant claims include alkyl substituents, e.g., methyl, on the phenyl ring A. The reference discloses many species wherein the phenyl ring is unsubstituted, see e.g., the species in col. 9, lines 24-25. The instant compounds differing from the reference compounds by having a methyl substituent are homologs of the reference compounds and it is well established in the art that compounds that are structurally homologous to the prior art compounds are *prima facie* obvious, in the absence of unexpected results. (emphasis added)

Applicants point out that the highlighted portion of the Examiner's argument quoted above is a bit misleading in that although WO 98/41525 discloses species wherein the phenyl ring is substituted by methoxy or hydroxy, the species in WO 98/41525 are not the same as the species of the instant application's claim 46 except for the methoxy or hydroxy group. That is, there isn't a series of species in WO 98/41525 that are exactly the same as the series of species in claim 46 of the instant application except the substituent on the phenyl group.

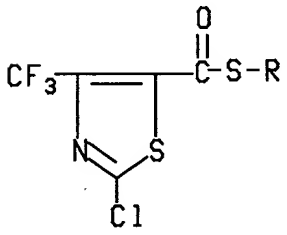
The Examiner has further noted the following at pages 7-8 of the instant Office Action:

> It is to be noted that rejection under 35 U.S.C. 103 is proper where the subject matter claimed "is not *identically* disclosed or described" in the prior art, and the prior art directs those skilled in the art to the compounds, with out any need for picking, choosing, and combining various disclosures. See *In re Shumann et al.*, 572 F2d 312, 315, 316, 197 USPQ 5, 8, (CCPA 1978). Further, the reference teaches integrin antagonistic activity for compounds, which is sufficient to one of ordinary skill to make the claimed compounds because similar properties are normally presumed when compounds are very close in structure. *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976). "The question under 35 U.S.C. 103 is not merely what the reference expressly teaches but what it would have suggested to one of ordinary skill in the art at the time the invention was made." See *In re Duel*, 51 F.3d at 1558, 34 USPQ2d at 1214. The closer the physical and chemical similarities between the claimed species or subgenus and any exemplary species or subgenus disclosed in the prior art, the greater the expectation that the claimed subject matter will function

> in an equivalent manner to the genus. See *In re Dillon,* 919 F.2d at 696, 16 USPQ2d at 1904. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne* 606 F2.d 303, 313, not only for what is expressly teaches but also for what it fairly suggests; all disclosures of prior art, including unpreferred embodiments, must be considered in determining obviousness. In re Burckel, 201 USPQ 67 (CCPA 1979).

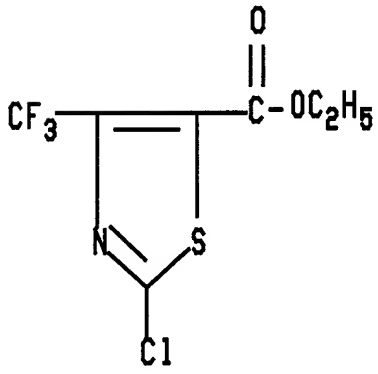
However, Applicants point out that the Court of Appeals, Federal Circuit stated in In re Grabiak that "there must be adequate support in the prior art for the ester/thioester change in structure, in order to complete the PTO's *prima facie* case and shift the burden of going forward to the applicant." In re Grabiak, 226 USPQ 870, 872, 1985. The Grabiak court made the above statement in light of the fact that both appellant's compounds and the prior art compounds were very similar in structure (see below) and had the same utility, namely, as herbicidal safeners.

Grabiak's compound



wherein R is $C_{1\text{-}5}$alkyl, phenyl or benzyl

Howe's Compound



Note that when the R substituent is ethyl in the Grabiak compound, that the only difference in structure between Grabiak and Howe is a single atom, namely, an oxygen atom versus a sulfur

atom. Hence, structural similarity and identical utility on its own cannot be the sole basis for a rejection under 35 U.S.C. § 103. Yet, the Examiner's rejection in the instant application under 35 U.S.C. § 103 is based upon such a premise.

Applicants submit that the Examiner must show motivation in WO 98/41525 to make the species of the instant application's claim 46. The Examiner has not pointed out such motivation. Accordingly, the rejection of claim 46 under 35 U.S.C. 103(a) over WO 98/41525 is obviated and should be withdrawn.

The Examiner has rejected claims 1-8, 10-11 and 46-47 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of U.S. Patent No. 6,001,839. Applicants note that the instant rejection may be overcome by the filing of a terminal disclaimer. Applicants point out that the instant application has the same chain of priority as the '839 patent and, thus, will expire on the same date. Applicants also note that both the '839 patent and the instant application are owned by the same owner. Applicants will submit a terminal disclaimer in the near future because Applicants are not in a position to file a terminal disclaimer at this time for the following reason. U.S. Patent No. 6,001,839 and the instant application (and other intellectual property) were purchased by Abbott Laboratories on March 2, 2001 from BASF Aktiengesellschaft, the assignee of record, and, therefore, Abbott Laboratories is the equitable owner of the instant application and the '839 patent. However, new assignment documents reflecting the transfer of ownership from BASF to Abbott have not yet been recorded with the USPTO Recordation Office. Therefore, Applicants and Applicants' attorney are not in a position to sign a terminal disclaimer. Applicants shall file new assignments and then follow-up by filing a terminal disclaimer in the instant application over the '839 patent. Submission of such a terminal disclaimer is not to be construed as an acquiescence to the Examiner's rejection of claim 46 over WO 98/41525, which Applicants maintain is a separate issue.

The Examiner has objected to claims 1 and 6, for the following informalities: the "and" in claim 1 that precedes the proviso clause should be deleted; and in claim 6, replace the "." in the middle of the claim with a ";". In response thereto, Applicants have effected both amendments. Accordingly, Applicants respectfully request that the objection to claims 1 and 6 be withdrawn.

No fees are due for the instant amendment since the total number of claims and the total number of independent claims after entry of the amendments hereinabove is not more than the total number of claims and the total number of independent claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 1-8, 10-11 and 46-51 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' attorney at the number noted below.

If a fee is deemed to be due for the instant submission, the Commissioner is hereby authorized to withdraw the amount due from USPTO Account No. 01-0025.

Date: Nov. 20, 2002

Respectfully submitted,

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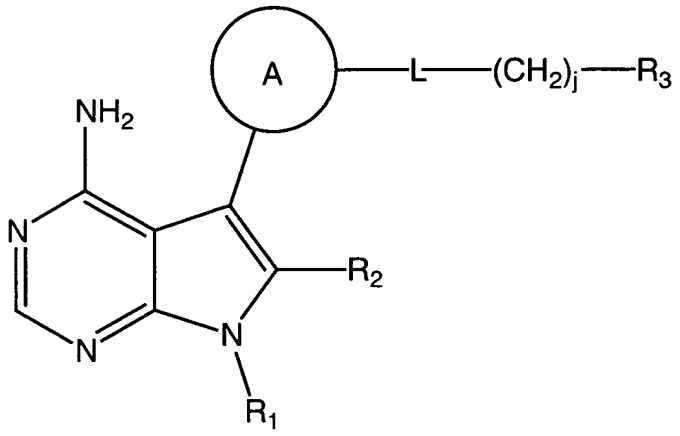
APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. (Thrice Amended) A compound represented by the following structural formula:



or pharmaceutically acceptable salts thereof, wherein:

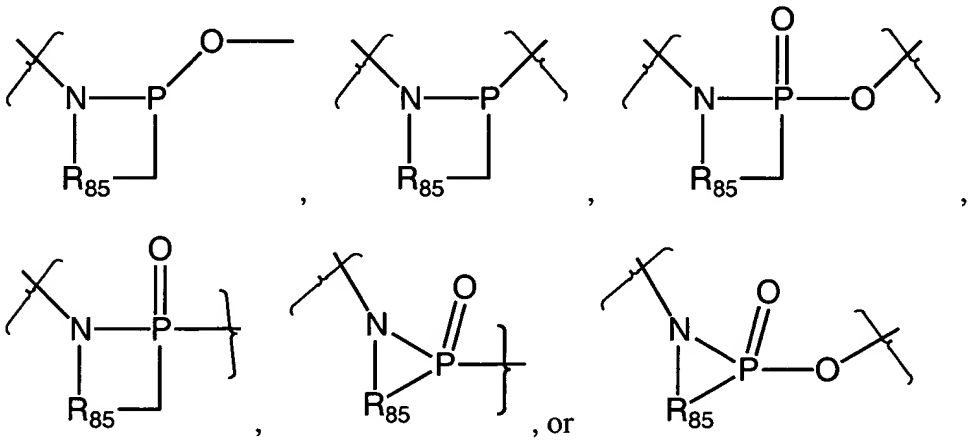
Ring A is a six membered aromatic ring or a five or six membered heteroaromatic ring which is substituted with one or more substituents selected from the group consisting of a substituted or unsubstituted aliphatic group, a halogen, a substituted or unsubstituted aromatic group, substituted or unsubstituted heteroaromatic group, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, cyano, nitro, $-NR_4R_5$, $-C(O)_2H$, a substituted or unsubstituted alkoxycarbonyl, $-C(O)_2$-haloalkyl, a substituted or unsubstituted alkylthio, a substituted or unsubstituted alkylsulfinyl, a substituted or unsubstituted alkylsulfonyl, a substituted or unsubstituted arylthio, a substituted or unsubstituted arylsulfinyl, a substituted or unsubstituted arylsulfonyl, a substituted or unsubstituted alkyl carbonyl, -C(O)-haloalkyl, a substituted or unsubstituted aryloxy, a substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylsulphonamido, trifluoromethylcarbonylamino, a substituted or unsubstituted alkynyl, a substituted or unsubstituted alkyl amido or alkylcarboxamido; a substituted or

unsubstituted aryl amido or arylcarboxamido, a substituted or unsubstituted styryl and a substituted or unsubstituted aralkyl amido or aralkylcarboxamido;

L is -S-; -S(O)-; -$S(O)_2$-; -N(C(O)OR)-; -N(C(O)R)-; -$N(SO_2R)$-; -CH_2O-; -CH_2S-; -$CH_2N(R)$-; -CH(NR)-; -$CH_2N(C(O)R)$)-; -$CH_2N(C(O)OR)$-; -$CH_2N(SO_2R)$-; -CH(NHR)-; -CH(NHC(O)R)-; -$CH(NHSO_2R)$-; -CH(NHC(O)OR)-; -CH(OC(O)R)-;-CH(OC(O)NHR)-; -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; [-$NHC(O)R_{130}$-;] -N(R)S(O)-; -$N(R)S(O)_2$-; [-$NHSO_2R_{130}$-;] -OC(O)N(R)-; -N(R)C(O)N(R)-; -NRC(O)O-; -S(O)N(R)-; -$S(O)_2N(R)$-; -N(C(O)R)S(O)-; -$N(C(O)R)S(O)_2$-; -N(R)S(O)N(R)-; -$N(R)S(O)_2N(R)$-; -C(O)N(R)C(O)-; -S(O)N(R)C(O)-; -$S(O)_2N(R)C(O)$-; -OS(O)N(R)-; -$OS(O)_2N(R)$-; -N(R)S(O)O-; -$N(R)S(O)_2O$-; -N(R)S(O)C(O)-; -$N(R)S(O)_2C(O)$-; -SON(C(O)R)-; -$SO_2N(C(O)R)$-; -N(R)SON(R)-; -$N(R)SO_2N(R)$-; -C(O)O-; -N(R)P(OR')O-; -N(R)P(OR')-; -N(R)P(O)(OR')O-; -N(R)P(O)(OR')-; -N(C(O)R)P(OR')O-; -N(C(O)R)P(OR')-; -N(C(O)R)P(O)(OR')O- or -N(C(O)R)P(OR')-, wherein R and R' are each, independently, -H, an acyl group, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted cycloalkyl group [and R_{130} is an aliphatic group]; or

L is -R_bN(R)$S(O)_2$-, -R_bN(R)P(O)-, or -R_bN(R)P(O)O-, wherein R_b is an alkylene group which when taken together with the sulphonamide, phosphinamide, or phosphonamide group to which it is bound forms a five or six membered ring fused to ring A; or

L is represented by one of the following structural formulas:



, , , , , or

wherein R_{85} taken together with the phosphinamide, or phophonamide is a 5-, 6-, or 7 -membered, aromatic, heteroaromatic or heterocycloalkyl ring system;

R_1 is -H, 2-phenyl-l,3-dioxan-5-yl, a C1-C6 alkyl group, a C3-C8 cycloalkyl group, a C5-C7 cycloalkenyl group or an optionally substituted phenyl(C1-C6 alkyl) group, wherein the alkyl, cycloalkyl and cycloalkenyl groups are optionally substituted by one or more groups of formula -OR^a; provided that -OR^a is not located on the carbon attached to nitrogen;

R^a is -H or a C1-C6 alkyl group or a C3-C6 cycloalkyl;

R_2 is -H, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted cycloalkyl, a halogen, -OH, cyano, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, a substituted or unsubstituted heterocycloalkyl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaralkyl, -NR_4R_5, or -$C(O)NR_4R_5$;

R_3 is a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted heterocycloalkyl; or L is -$NRSO_2$-, -NRC(O)-, -NRC(O)O-, -$S(O)_2NR$-, -C(O)NR- or -OC(O)NR-, and R_3 is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl or substituted or unsubstituted aralkyl;

provided that j is 0 when L is -CH_2NR-, -C(O)NR- or -NRC(O)- and R_3 is azacycloalkyl or azaheteroaryl; [and]

R_4, R_5 and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

R_4 and R_5 are each, independently, -H, azabicycloalkyl, a substituted or unsubstituted alkyl group or Y-Z;

Y is selected from the group consisting of -C(O)-, -$(CH_2)_p$-, -$S(O)_2$-, -C(O)O-, -SO_2NH-, -CONH-, $(CH_2)_pO$-, -$(CH_2)_pNH$-, -$(CH_2)_pS$-, -$(CH_2)_pS(O)$-, and -$(CH_2)S(O)_2$-;

p is an integer from 0 to 6;

Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; and

j an integer from 0 to 6.

6. (Twice Amended) The compound of Claim 5 wherein ring A is substituted with one or more substituent selected from the group consisting of F, CI, Br, I, CH_3, NO_2, CN, CO_2CH_3, CF_3, t-butyl, pyridyl, substituted or unsubstituted oxazolyl, substituted or unsubstituted benzyl, substituted or unsubstituted benzenesulfonyl, substituted or unsubstituted phenoxy, substituted or unsubstituted phenyl, substituted or unsubstituted amino, carboxyl, substituted or unsubstituted tetrazolyl, styryl, -S-(substituted or unsubstituted aryl), -S-(substituted or unsubstituted heteroaryl), substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocycloalkyl, alkynyl, $-C(O)NR_fR_g$, R_c and CH_2OR_c[.];

R_f, R_g and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

R_f and R_g are each, independently, -H, a substituted or unsubstituted aliphatic group or a substituted or unsubstituted aromatic group; and

R_c is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, $-W-(CH_2)_t-NR_dR_e$, $-W-(CH_2)_t$-O-alkyl, $-W-(CH_2)_t$-S-alkyl, or $-W-(CH_2)_t-OH$;

t is an integer from 0 to 6;

W is a bond or -O-, -S-, -S(O)-, $-S(O)_2-$, or $-NR_k-$;

R_k is -H or alkyl; and

R_d, R_e and the nitrogen atom to which they are attached together form a 3, 4, 5, 6 or 7-membered substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

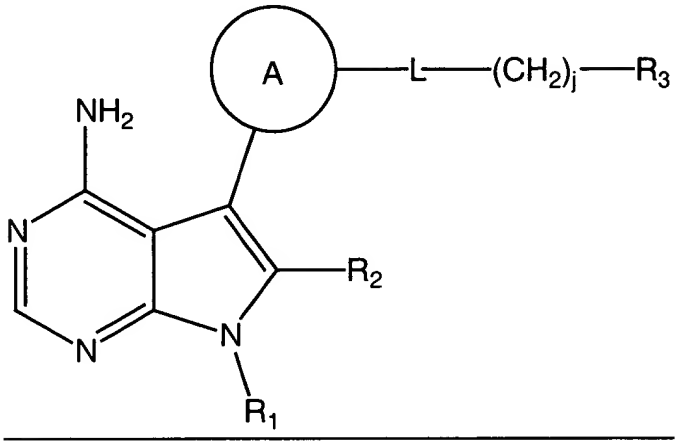
R_d and R_e are each, independently, -H, alkyl, alkanoyl, or -K-D;

K is $-S(O)_2-$, -C(O)-, -C(O)NH-, $-C(O)_2-$, or a direct bond;

D is a substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaromatic group, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted aminocycloalkyl, $COOR_i$, or a substituted or unsubstituted alkyl; and

R_i is a substituted or unsubstituted aliphatic group or a substituted or unsubstituted aromatic group.

11. (Thrice Amended) [The] A compound [of Claim 1,] represented by the following structural formula



or pharmaceutically acceptable salts thereof, wherein:

Ring A is a six membered aromatic ring or a five or six membered heteroaromatic ring which is substituted with one or more substituents selected from the group consisting of a substituted or unsubstituted aliphatic group, a halogen, a substituted or unsubstituted aromatic group, substituted or unsubstituted heteroaromatic group, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, cyano, nitro, $-NR_4R_5$, $-C(O)_2H$, a substituted or unsubstituted alkoxycarbonyl, $-C(O)_2$-haloalkyl, a substituted or unsubstituted alkylthio, a substituted or unsubstituted alkylsulfinyl, a substituted or unsubstituted alkylsulfonyl, a substituted or unsubstituted arylthio, a substituted or unsubstituted arylsulfinyl, a substituted or unsubstituted arylsulfonyl, a substituted or unsubstituted alkyl carbonyl, -C(O)-haloalkyl, a substituted or unsubstituted aryloxy, a substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylsulphonamido, trifluoromethylcarbonylamino, a substituted or unsubstituted alkynyl, a substituted or unsubstituted alkyl amido or alkylcarboxamido; a substituted or unsubstituted aryl amido or arylcarboxamido, a substituted or unsubstituted styryl and a substituted or unsubstituted aralkyl amido or aralkylcarboxamido;

wherein L is $-NHSO_2R-$, [$-NHSO_2R_{130}-$,] -NHC(O)O-, or $-NHC(O)R-$ [$-NHC(O)R_{130}-$]

wherein R is -H, an acyl group, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted cycloalkyl group; or

R_1 is -H, 2-phenyl-l,3-dioxan-5-yl, a C1-C6 alkyl group, a C3-C8 cycloalkyl group, a C5-C7 cycloalkenyl group or an optionally substituted phenyl(C1-C6 alkyl) group, wherein the alkyl, cycloalkyl and cycloalkenyl groups are optionally substituted by one or more groups of formula -OR^a; provided that -OR^a is not located on the carbon attached to nitrogen;

R^a is -H or a C1-C6 alkyl group or a C3-C6 cycloalkyl;

R_2 is -H, a substituted or unsubstituted aliphatic group, a substituted or unsubstituted cycloalkyl, a halogen, -OH, cyano, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, a substituted or unsubstituted heterocycloalkyl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaralkyl, -NR_4R_5, or -$C(O)NR_4R_5$;

R_3 is a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aromatic group, a substituted or unsubstituted heteroaromatic group, or a substituted or unsubstituted heterocycloalkyl; or L is -$NRSO_2$-, -NRC(O)-, -NRC(O)O-, -$S(O)_2NR$-, -C(O)NR- or -OC(O)NR-, and R_3 is substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl or substituted or unsubstituted aralkyl; and

R_4, R_5 and the nitrogen atom together form a 3, 4, 5, 6 or 7-membered, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted heterobicycloalkyl or a substituted or unsubstituted heteroaromatic; or

R_4 and R_5 are each, independently, -H, azabicycloalkyl, a substituted or unsubstituted alkyl group or Y-Z;

Y is selected from the group consisting of -C(O)-, -$(CH_2)_p$-, -$S(O)_2$-, -C(O)O-, -SO_2NH-, -CONH-, $(CH_2)_pO$-, -$(CH_2)_pNH$-, -$(CH_2)_pS$-, -$(CH_2)_pS(O)$-, and -$(CH_2)S(O)_2$-;

p is an integer from 0 to 6;

Z is a substituted or unsubstituted alkyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heterocycloalkyl group; and

j an integer from 0 to 6.